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4. Title of the invention — ENCAPSULATED RADIOACTIVE NUCLIDE MICROPARTICLES AND METHODS FOR THEIR PRODUCTION

5. Name of your agent *(if you have one)* — MEWBURN ELLIS

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ENCAPSULATED RADIOACTIVE NUCLIDE MICROPARTICLES AND METHODS FOR THEIR PRODUCTION

There has been great interest in the incorporation of foreign materials into enclosed nano-carbon cages. This interest has been driven by the potential applications of these filled carbon capsules, which lie in areas as diverse as optical, electronic, storage, magnetic recording materials, and nuclear medicine. In particular, carbon (onion-shell) structures of extreme strength may offer excellent protection to their encapsulated nanomaterials for applications. In addition, the close packing structures of the carbon shells do not allow exchange of molecules/materials from inner cores to the external environment, hence materials of extremely reactive (air sensitive) or hazardous (radioactive) nature can be safely caged in the carbon-enclosed structures.

According to this invention, a novel methodology for the encapsulation of radioactive elements within the carbon cage is provided. This simple technique allows production of macroscopic quantities of quasi-spherical graphitic/fullerenic shells (carbon onions) that can encapsulate nanoparticles containing radioactive element(s) of a very narrow range of particle diameters.

We believe the method may offer new routes for safe handling/disposal of radioactive substances and the carbon coated nano-radioactive products may find applications in medical imaging or radiotherapy.

The idea of using carbon caged structures as molecular containers dates back many years [1,2] before the actual discovery of fullerene and related structures. Research in this area is chiefly driven by the potential applications of filled nanocapsules in areas such as electronics (quantum dots and wires), magnetic data storage, xerographics, lubrication, sensors and medicinal materials [3-5]. So far, several groups have succeeded in encapsulating various nanosized materials into fullerene structures by either using Krätschmer-Huffman arc [6,7], laser [8] or electron irradiation methods [9] during the fullerene synthesis or by creating an 'opening' in the carbon caged structures using chemical methods [10-12] prior to filling. Yields of the endohedral metallofullerenes synthesis [8] tend to be low and there are doubts about stability. Filled polygonal shaped carbon nanoparticles and nanotubes appear to be more promising from the point of view of applications. The techniques currently used to synthesise these structures include modifications of Krätschmer-Huffman arc method and methods involving heat treatment of

impregnated microporous carbon [13,14]. It is noted that there is no macroscopic synthetic method yet developed for the preparation of filled carbon onions (quasi-spherical graphitic shells) although minuscule amounts were produced through irradiation of amorphous carbon, nanotubes or nanoparticles with foreign atoms with an intense electron beam [9]. No reported work has been found on the preparation of total carbon encapsulation of radioactive nanoparticles.

In nuclear medicine, the choice and form of radionuclides should be carefully chosen. The choice of a radionuclide for imaging purposes is chiefly dictated by the necessity of minimizing the radiation dose to the patient and the detection characteristics of present-day nuclear medicine instrumentation. The forms should preferably be non-toxic in the desired amounts, and would not directly involve in the patient's physiological body mechanisms. The form, structure and morphology and concentration of the radioactive material will also affect the imaging quality (small particle size will give better imaging quality i.e. smaller pixels. This invention describes a novel, easy, convenient method for the synthesis of complete carbon encapsulated radionuclides with a narrow particle size distribution suitable for diagnostic imaging and therapeutic

applications. The impermeable carbon coatings offer total isolation of the enclosed nuclides from the environment.

The novel method described herein is concerned with a methodology for the production of a complete carbon encapsulated radioactive material with a small range of particle size. We believe these materials produced from the method will find applications in lung ventilation and lung perfusion imaging and other diagnostic and radiotherapy areas.

This method may be suitable to encapsulate a wide range of radionuclides (parental or daughter nuclides) with different emitted radiation and decay times.

Typical example, Half-life:	(i)	^{99}Mo 67 hours	→	^{99m}Tc 6 hours	→	^{99}Tc long	→ ^{99}Ru stable
Half-life	(ii)	^{113}Sn 115 days	→	^{113m}Sn 1.67 hours	→	^{113}In stable	
Half-life	(iii)	^{68}Ge 275 days	→	^{68}Ga 1.1 hours	→	^{68}Zn stable	
Half-life	(iv)	^{81}Rb 4.7 hours	→	^{81m}Kr 13 seconds	→	^{81}Kr stable	

Technetium-99m (^{99m}Tc) has excellent physical characteristics for diagnostic imaging having a half-life of 6 h and emitting gamma-ray photons at an energy of 140 keV which are suitable for detection with a gamma camera. ^{99m}Tc is easily obtained from a commercially available

$^{99}Mo/^{99m}Tc$ generator. ^{99}Mo is a fission product which is obtainable in a carrier-free form with a high specific activity. It has a half-life of 66.02 h and decays to ^{99m}Tc by ß- emission, which decays by isomeric transition to ^{99}Tc. In commercially available generators ^{99}Mo is absorbed onto an alumina column. Elution of the generator with 0.9% sodium chloride solution elutes the ^{99m}Tc in the form of sodium pertechnetate ($Na^{99m}TcO_4$) leaving the ^{99}Mo bound to the column[15]. $^{99}Mo/^{99m}Tc$ generators are generally purchased by hospitals on a weekly basis and have a working life of one week. ^{99m}Tc is incorporated in a variety of chemical forms for oral intake, injection or for lung ventilation/perfusion.

For lung imaging "Technegas" has been developed. It is an ultrafine ^{99m}TC-labelled aerosol introduced by W. Burch [22] in 1986. The small radioactive particles (nanometric in size) in a Technegas aerosol result in better clinical images than those obtained from other radioactive aerosols. It is known that the size and the content of the Tc particle in the aerosol can critically affect the quality of the images. The size of the aerosol particles also determines the site of lung deposition (bronchial and alveolar regions), subsequent modes and rates of clearance and hence will affect the diagnostic information obtained. More recent work, using

electron microscopy, has shown that ^{99m}Tc particles in Technegas are in fact relatively large crystals of over 100 nm in diameter. Another problem that arises with the production of Technegas is that significant quantities of ^{99m}Tc are incompletely protected in the carbon matrix. This leads to leaching of radioactive ^{99m}Tc to body fluids hence resulting in the undesirable appearance of ^{99m}Tc in the saliva, oesophagus, stomach and thyroid gland and thus degrading the quality of the images. In addition the high cost of purchasing the commercial Technegas generator has limited its use in many centres.

Our method involves the preparation of graphitic-encapsulated microparticles, more particularly nanoparticles, by the dissolution of a source or sources of iron, carbon and a heteroatom (usually N, but B, P, S or O for example may be used) in a polar solvent at elevated temperature; partially decomposing the iron compound to an insoluble iron oxygen species; size controlling and stabilizing the partially oxidised iron species by use of a surfactant; and pyrolyzing the stabilized species to yield a metallic core encapsulated by a graphitic/hetero shell. To form a radionuclide-containing particle, a salt or complex of a radionuclide is also present. It is found that during the partial decomposition of the iron compound, especially in the

absence of oxygen, the radionuclide is incorporated into the core.

Since the graphitic encapsulation derives primarily from the carbon source, regulation of the carbon:iron ratio can help determine the numbers of encapsulating layers around a core; this in turn may act as a modulator or regulator of the radiation emitted from a radionuclide in the core.

The invention provides also radionuclide-covered microparticles, especially nanoparticles, of which an encapsulating shell around the core is of graphitic/hetero layers. Usually the hetero atoms will be N.

In more detail some of the most important synthesis steps in obtaining the desired products have been elucidated. These include the fact that iron species (catalyst) catalyse formation of enclosed graphitic structure from its attached cyanide ligand (or carbon and nitrogen containing ligand, stabiliser) upon heating, which will subsequently enclose the iron particle forming completely encapsulated particles. Prior heat treatment control in particle size is important in order to make encapsulated nanosized particles. We therefore show that adding surfactants or polymers controls the particle sizes and stabilisation of insoluble iron and cyanide-

containing nanoparticles when soluble iron cyanide species is partially decomposed in a high-boiling polar solvent. This is based on the fact that the polymer/surfactant adsorbs at the surface of the newly formed nano-particles forming micellar protection so preventing aggregation. In other contexts, stabilisation of colloid in a polymer solution is a well-established technique typically in paint and inkjet technologies. Thus, we show that controlled size of Fe cyanide containing nanoparticles stabilised with adsorbed polymers/surfactants is a most important step before the radioactive element incorporation. The incorporation of foreign element(s) to the stabilised iron containing particles can be subsequently performed by developing specific interactions (chemical linkage, ion-exchange, redox attachment, etc) with the Fe(II) containing particles. Finally, after the removal of solvents followed by heat treatment the stabilised nanoparticles containing iron and foreign atoms with a narrow size distribution will give rise to the desired products. It is noted that the residue cyanide species in the particles will provide the carbon source for the formation of enclosed graphitic structure. We show that Re species can be successfully incorporated into the carbon-encapsulated iron containing nanoparticles via

using ReO_4^- . This clearly implies that the incorporation of ^{99m}Tc is made possible by this technique because of their almost identical chemical properties (lanthanide contraction). Other radioactive elements such as ^{99m}Mo, ^{113}Sn can similarly be incorporated into this novel carrier (surfactant stabilised iron(oxo) cyanide nanoparticles) by employing similar chemistry.

An object of the invention is to develop a low temperature solution method for encapsulation of radioactive nono-particles/clusters with a fine control in particle size. There are many advantages in the safe handling/disposal of radioactive materials if the materials are stored in an imperative carbon coating. Early work suggested it was difficult to carry out complete encapsulation of material with graphitic carbon unless the temperature rose above the vaporisation temperatures of graphite (>250°C) during electric arc excitation [22]. However, there are many disadvantages associated with the extremely high temperature synthetic method especially regarding to the difficulty in controlling the particle size. Complete carbon encapsulation over radioactive nanoparticles thus may require a high temperature since amorphous carbon atoms do not offer total protection to these particle against leaching. The crystallisation of amorphous carbon atoms

into complete graphitic protective capsule structures (graphitic carbon shells) is known to take place at minimum temperature of 2500°C [25]. However, the alternative would be to induce graphitisation at low temperatures by the use of catalyst. The phenomenon of low-temperature (<700°C) "catalytic graphitisation" from a different variety of carbon sources over Fe, Co, Ni, Cr, has been known for many years. Here we demonstrate clearly that the formation of iron or iron carbide encapsulated in carbon shells from heat treatments of stabilised iron(II) (oxo) cyanide species can be achieved. The cyanide species provide carbon source for the formation of enclosed graphitic shells. This indicates an effective catalytic carbonisation over the iron materials.

In summary, we report the (a) effectiveness of using catalytic component (Fe, Ni, Co cyanides) to form well-defined sized nanoparticles in a high boiling polar solvent (with stabiliser) during their cyanide decomposition; (b) incorporation of foreign atoms (radioactive atom, such as ^{99m}Tc) into the iron(II) oxo-cyanide nanoparticle aggregates can be achieved using the oxidative $^{99m}TcO_4$ ions through a fast redox trapping mechanism; (c) thermal decomposition of these colloidal

particles (with cyanide) result in the enclosed graphitic structure embracing radioactive element(s).

In the drawings:

Figure 1 is an electron micrograph showing a large discrete iron-containing particle encapsulated within graphitic carbon shells prepared from decomposition of iron cyanide particle (scale bar = 50 nm) in nitrogen;

Figure 2 shows the powder X-ray diffraction (XRD) spectrum of pure $Fe^{III}_4[Fe^{II}(CN)_6]_3$ salt acting as a precursor;

Figures 3 and 4 show the powder X-ray diffraction (XRD) spectra of partial air decomposed $Fe^{III}_4[Fe^{II}(CN)_6]_3$ in refluxing dioctylether (Figure 3: small amount of dissolveed oxygen in dioctylether; Figure 4: oxygen continuously purging through the system);

Figure 5 (a TEM micrograph) shows the colloidal stable iron-oxo-cyanide containing nanoparticles obtained via refluxing 0.86 g $Fe^{III}_4[Fe^{II}(CN)_6]_3$ salt in 40 ml dioctylether solvent with adding oleic acid (20 ml). Small but homogeneous sized organic stabilised nanoparticles (~ 10 nm) are clearly visible (nanosize particles giving a super-lattice packing);

Figure 6 is a typical high resolution transmission electron micrograph (lattice image) showing iron nanoparticles with the interplanar spacing of 2.1 $\pm$ 0.5 Å

corresponding to (111) of fcc Fe (cementite) encapsulated in concentric quasi-spherical graphitic shells of 3.4 x 10^{-8m} (scale bar = 5 nm);

Figure 7 is the EDX spectrum of Re-incorporated stabilised Fe nanoparticles which show the selected area rich in iron and rhenium; Cu peaks arise from the copper grids;

Figure 8 shows the corresponding high-resolution TEM image of Re-incorporated stabilised Fe nanoparticles with very well defined size and shape (as Figure 7) (scale bar = 20 nm);

Figure 9 is a high resolution TEM image of a spherical graphitic shell structure (2-5 layers) filled with Fe and Re containing nanoparticles after applying heat treatments to the same in Figure 8 (scale bar = 20 nm); and

Figure 10 shows the result of irradiation of amorphous carbon with intense electron beam in TEM showing it to spherical graphitic concentric shells (onions); and a diagrammatic model attached (scale bar 100 x 10^{-8m}).

2. Experimental and Results

Example 1: Synthesis of Carbon Encapsulated Iron Particles (comparative)

A sample of Iron (III) Ferrocyanide (purity >99.9%) obtained from Sigma plc, was transferred into a quartz tube with one end plugged with quartz wool. The filled tube, which was placed in the tube furnace, was first heated to 200°C, (Heating Rate: 5°C/Min, Duration: 2h), and then finally to 900°C, (Heating Rate: 10°C/Min; Duration: 3h), in N_2 atmosphere (Approx, Flow Rate: 0.9 L/min). The black materials formed were stored in a sample vial. Elemental analyses from the EDX analysis and microanalysis showed that the sample after the heat treatments contained mainly C, Fe and a small amount of nitrogen (2-4%), which was scratched off the tube and examined by TEM. The TEM micrograph in Figure 1 shows that an iron-containing particle (iron and iron carbides) is encapsulated by graphitic carbon shells (onion structure) though the sizes of most of these encapsulated particles are very large (>0.1μm). Thus, it is clear that iron catalyses formation of enclosed graphitic structure from cyanide- or carbon-nitrogen-containing ligand. Other metals such as alkali or alkaline earths are unable to catalyse these enclosed graphitic structures from their cyanide salts, nor are iron species without using nitrogen containing salt/ligand/stabiliser.

Example 2: Synthesis of Carbon Encapsulated Iron Nanoparticles:

Example 1 discloses the use of iron cyanide salt for the formation of enclosed graphitic structure embracing iron particle however no control in particle size was achieved. Here we describe the use of a polar high boiling solvent (such as dioctyl ether-boiling point 287°C) to dissolve the iron ferrocyanide compound at refluxing temperature (the compound is fairly soluble in the solvent at elevated temperature) giving intense blue colour solution. Iron-containing cyanide compounds are known to decompose at about 200-250°C [23,24]. In the presence of dissolved oxygen (air) with purging the system with an air stream the $Fe^{II}(CN)_6^{4-}$ from the $Fe^{III}_4[Fe^{II}(CN)_6]_3$ salt will decompose to $Fe(CN)_{2-3}O_{1-2}^{n-}$ losing the cyanide species but simultaneously replacing them with oxygen species [23]. This will ultimately lead to precipitating of iron oxide that is insoluble in the solvent. Figure 2 shows the powder X-ray diffraction (XRD) of the pure $Fe^{III}_4[Fe^{II}(CN)_6]_3$ salt. Iron oxide structure (magnetite, Fe_3O_4) is formed from the partial iron cyanide air-decomposition giving mixed phases in the XRD patterns, the extent of the decomposition depends on the oxygen availability and duration of the treatment (Figures 3 and 4). An organic surfactant/stabiliser

(such as oleic acid, polyvinylpyrrolidone, PVP) stabilises the partially oxidised iron cyanide species against precipitation from the solution. Figure 5 (TEM micrograph) shows the colloidal stable iron-oxo-cyanide containing nanoparticles obtained via refluxing 0.86g $Fe^{III}_4[Fe^{II}(CN)_6]_3$ salt in 40 ml dioctylether solvent with adding oleic acid (20 ml). Small but homogeneous particle size (nanosize particles giving a super-lattice packing) is obtained using this preparative mixture. There is a clear indication that the size of the particle can also be finely controlled by tailoring the ratio of oleic acid to the iron compound. Oleic acid being with a polar head group (acid group) and a double bond in the middle of the molecule will act as surfactant. It is envisaged that the double bond will interact strongly with the iron species in the inner core of a micelle while its polar head will face outwards forming a normal phase micelle in this polar solvent. Hence the micellar structure provides a fine control in particle size. It is shown that application of the same heat treatment mentioned in Example 1 to the colloidal iron containing particles produces iron/iron carbide particle encapsulated in the enclosed graphitic carbon shelled structure (Figure 6).

Example 3: Synthesis of Carbon Encapsulated Nanoparticles containing Radioactive or Related Elements:

Example 2 shows that molecular oxygen from air can partially oxidise the iron cyanide compound in dioctylether at elevated temperatures. Adding a small quantity of sodium perrhenate (inorganic oxidant) to the mixture as the described in Table 1, can also oxidise the iron (II) cyanide species. Experimental details for typical synthesis is described below:

Chemical Name	**Chemical Formula**	**Mol.Wt.**	**Act. Wt/g**	**Features**
Sodium Perrhenate	$NaReO_4$	273	**0.28**	White Crystals
Iron (III) Ferrocyanide	$Fe^{III}_4[Fe^{II}(CN)_6]_3$	859.25	**0.86**	Blue powder
Dioctylether	$[CH_3(CH)_2)_7]_2O$	242.45	**40 ml**	Clear Liquid
Oleic acid	$CH_3(CH_2)_7CH=CH(CH_2)_7COOH$	282	**20 ml**	-

Table 1. The starting materials. All the materials were used as supplied by Aldrich.

The chemicals shown above, see Table 1, were mixed in a 3-necked round bottom flask using a magnetic stirrer bar. Before the mixture was heated up to 290°C for 18h, a gentle stream of nitrogen gas was bubbled directly into the mixture for 30 min. Nitrogen gas was continuously bubbled into mixture during the reaction. The black mixture formed was allowed to cool to room temperature.

20 ml of Ethanol was added to the product before the resultant mixture was being centrifuged at 4000 rpm for 20 min. This procedure was repeated 3 times. The blue resultant solids were allowed to air dried in the fume cupboard.

Because of the d- electron configuration (lanthanide contraction) rhenium (Re) shows almost identical chemical properties as Technetium (Tc). Typically, the reduction potentials of the ReO_4^- and $^{99m}TcO_4^-$ species are of about 0.7 V (V versus NHE). It is reported that a fast rate of reductive deposition of TcO_4^- is obtained over small solid magnetite[39] (iron oxide). $^{99m}TcO_4^-$ for its reductive deposition onto the organic stabilised nano-iron containing particles as described in this process, followed by heat treatment will make a carbon encapsulated particle containing radioactive ^{99m}Tc element. As a result, the small but defined dimensions of the iron core (as a catalyst) can incorporate a significant amount of radioactive ^{99m}Tc into the final carbon encapsulated particles for imaging, storage and radio-therapeutic applications by this technique.

After heat treatment (which may be carried out in various stages or steps) the finely colloid enclosed graphitic structures are observed embracing both the iron

and rhenium elements with the carbon enclosed shells (Figure 9).

Carbon encapsulation is achieved by heating the particles in nitrogen as follows. The as-synthesised sample was first transferred into a quartz tube with one end plugged with quartz wool. The filled tube, which was placed in the tube furnace, was first heated to 200°C, (Heating Rate: 5°C/Min, Duration: 2h), and then finally to 900°C, (Heating Rate: 10°C/Min; Duration: 3h), in N_2 atmosphere (Approx, Flow Rate: 0.9 L/min). The black materials were stored in a sample vial.

Hence, during the decomposition of iron cyanide at elevated temperature, in the absence of air, the oxygen species will be transferred from the ReO_4^- species to the $Fe^{II}(CN)_6^{4-}$ (Re(+7) will be reduced while simultaneously oxidising the Fe^{2+}) leading to incorporation of the Re species into the stabilised very well-defined, nano-sized iron (oxo) cyanide particles (see EDX analysis in Figure 7 and the TEM micrograph in Figure 8 prior heat treatments).

Characterisation of the Product:

High resolution TEM micrographs indicate that the iron-containing particles were mainly single nano-crystals of γ-Fe metal(confirmed by XRD) although Fe_3C

crystals as the inner cores were sometimes observed from the TEM lattice imaging. Detailed examination the quasi-spherical carbon structures showed that in many cases, carbon lattice fringes (ca. 3.4Å) could be traced continuously yielding, quite surprisingly, hollow concentric carbon shelled structures. No prolonged exposure of the selected area to the electron beam was ensured (<60 seconds) hence the possibility of onions structure formation due to electron beam illumination is rejected. We found some complete filling but more frequently partial filling of the encapsulated iron particles to the carbon cages and there was no obvious preferred lattice fringe orientation with respect to the particle and the carbon layers. It is interesting to note that these highly ordered quasi-spherical concentric graphitic shells structures produced from iron cyanide decomposition are clearly different from tubular or polyhedral carbon structures. Formation of tubular/filamental graphitic carbons is well known to occur when a carbon source (i.e. hydrocarbon gas) is in contact with iron particles at high temperatures [15]. Polyhedral nanoparticles of central cavities of varying sizes were also observed when amorphous carbons were exposed to high temperatures [16]. It is also noted that extremely small quantities of γ-Fe nano-metal

crystallites encapsulated in polyhedral nanoparticles [17] were produced in a large amount of carbonanceous debris using the 'stuffed anode' modified Krateschmer-Huffman method where significant quantities of carbon nanotubes or 'sea urchin' structures [18] (carbon nanotubes grow radially fromthe metal nanocrystal) were also found. None of these structures were however seen in our sample. We note that our quasi-spherical graphitic shell structures rather closely resemble to the 'carbon onions' (refer to Figure 10) reported by Ugarte who applied an intense electron beam irradiation on carbon nanotubes for the conversion [19], although structurally less perfect than his. The perfect onion is thought to compose of giant fullerenes giving perfect concentric shells with a quasi-spherical structure. Subsequent work [20] demonstrated 'carbon onions' are highly unstable when not being irradiated in an electron beam and will collapse into disordered, quite often faceted configuration though still spheroidal structure somewhat akin to the structures observed.

Here, we have shown that heating the iron(oxo) cyanide nanoparticles (with or without foreign atoms) at 900°C results in graphitisation and the formation of many iron containing nanoparticles encapsulated in quasi-spherical graphitic shell. Presumably, the iron

nanoparticles were formed from the reduction of iron oxide with the nearby cyanide source during the carbonisation process.

The phenomenon of 'catalytic' graphitisation is a well-known one [11], but the mechanism in which graphitisation is promoted by the presence of a second phase is not well understood. In some cases, it is believed that the carbon is dissolved in the metal or metal carbide and re-precipitated as graphite. In other cases the metal or metal carbide particles may simply act as templates for the epitaxial growth of graphite. However, in all these cases, only long graphitic tubular or filamental forms of carbons and polyhedral nanoparticles are formed. The exclusive formation of highly ordered quasi-spherical graphitic nanocapsule structures indicative of 'fullerene-like structure' in our case however, has not been reported. It may be possible that some nitrogen (residue of cyanide decomposition) resulting from the decomposition of cyanide species may play an important role in self-assembling the carbon atoms into corresponding quasi-spherical structure under our reaction conditions. Nitrogen (non-sp2) adopts different structure as the carbon (sp2) hence its incorporation into carbon graphene layer (all C is in sp2 hybridization) might be

responsible for the curvature of the graphitic planes resulting in the particle encapsulation.

The present method for the formation of enclosed graphitic carbon structure embracing iron nanoparticle at very mild temperatures (900°C) is unprecedented. Thus, iron filled spherical carbon nanocapsules of a very narrow size distribution in macroscopic quantities by the controlled decomposition of cyanide-containing species could be prepared. Prior to pyrolysis, using surfactant/polymer as stabiliser could provide a fine control of particle size. This is based on the observation that the polymer/surfactant adsorbs at the surface of the newly formed nano-particles through the formation of surface active micellar aggregates so preventing aggregation of nanoparticle in solvent. The internal space is filled with an inorganic iron (oxo) cyanide nanoparticle aggregates with defined dimensions which are in turn controlled by the micellar dimensions. Further immobilisation of other foreign atoms onto the nanoparticle aggregates can be carried out. Here, we show that Re element can be incorporated into the final product, clearly suggesting that ^{99m}Tc can be incorporated in a similar manner. Thus, the controlled carbonisation of these iron containing nano-assemblies with cyanide species will act as the novel carrier which could open up

a new avenue for preparing carbon nanocapsules filled with specific radioactive element(s).

There are considerable benefits of forming total carbon encapsulated radionuclides that are well suited for medical diagnosis and therapeutic purposes. The potential beneficiaries will be to patients with lung disease using the carbon encapsulated ^{99m}Tc-Fe nano-particles described herein. For example, pulmonary embolism is a major cause of morbidity and mortality. It is estimated to account for approximately 21,000 deaths annually in England and Wales and over 200,000 in the USA. Early treatment by anticoagulation could save life, but it can sometimes be hazardous; a reliable means of diagnosis is therefore essential. The new technology for producing diagnostic or therapeutic material could provide rapid and efficient diagnosis suitable for patients with this or other pulmonary disease, hence improving life expectancy and quality.

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CLAIMS

1. Method for the preparation of encapsulated microparticles which includes dissolving a source or sources of iron, carbon and a heteroatom (usually N, but B, P, S or O for example may be used) in a polar solvent partially decomposing the iron compound at an elevated temperature to insoluble iron oxygen-containing particles; size controlling and stabilizing the partially oxidized iron species and pyrolysing the stabilized species to yield a metallic core encapsulated by a graphitic/hetero shell.

2. Method according to claim 1, wherein a salt or complex of a radionuclide is also present in the solvent medium.

3. Method according to claim 1 or claim 2, wherein a surfactant is present to effect the stabilizing.

4. Method according to any one of the preceding claims, wherein the size of microparticles are in the range of 5 μm to 50 μn.

5. Microparticles having a core containing a radionuclide encapsulated by a graphitic shell.

6. Microparticles according to claim 5, wherein the shell includes heteroatoms such that layers of the shell are curved.

7. Microparticles according to claim 5 or claim 6, wherein the heteroatoms are N.

8. Microparticles according to any one of claims 5 to 7 which are nanoparticles.

Figure 1

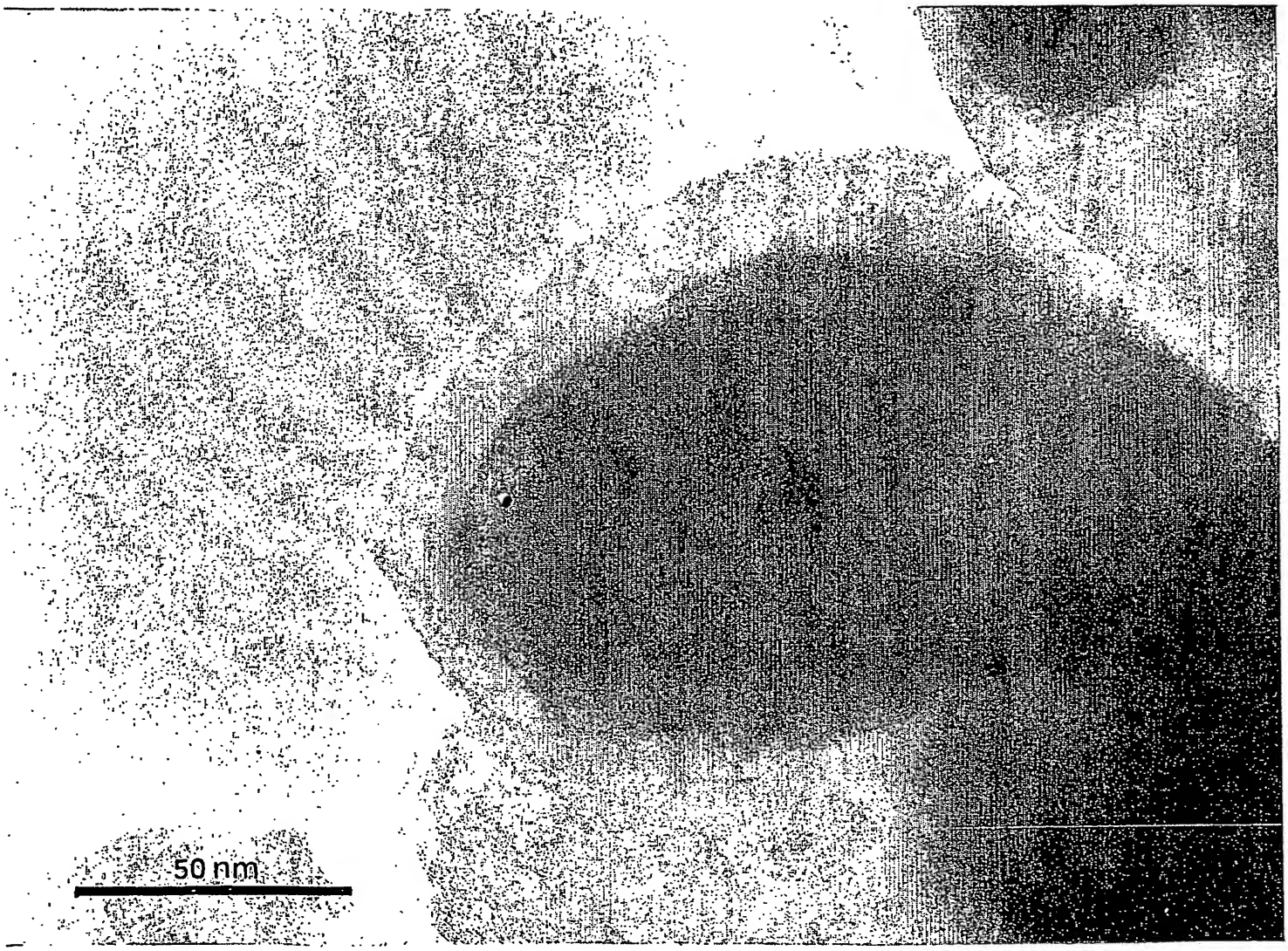

Figure 7

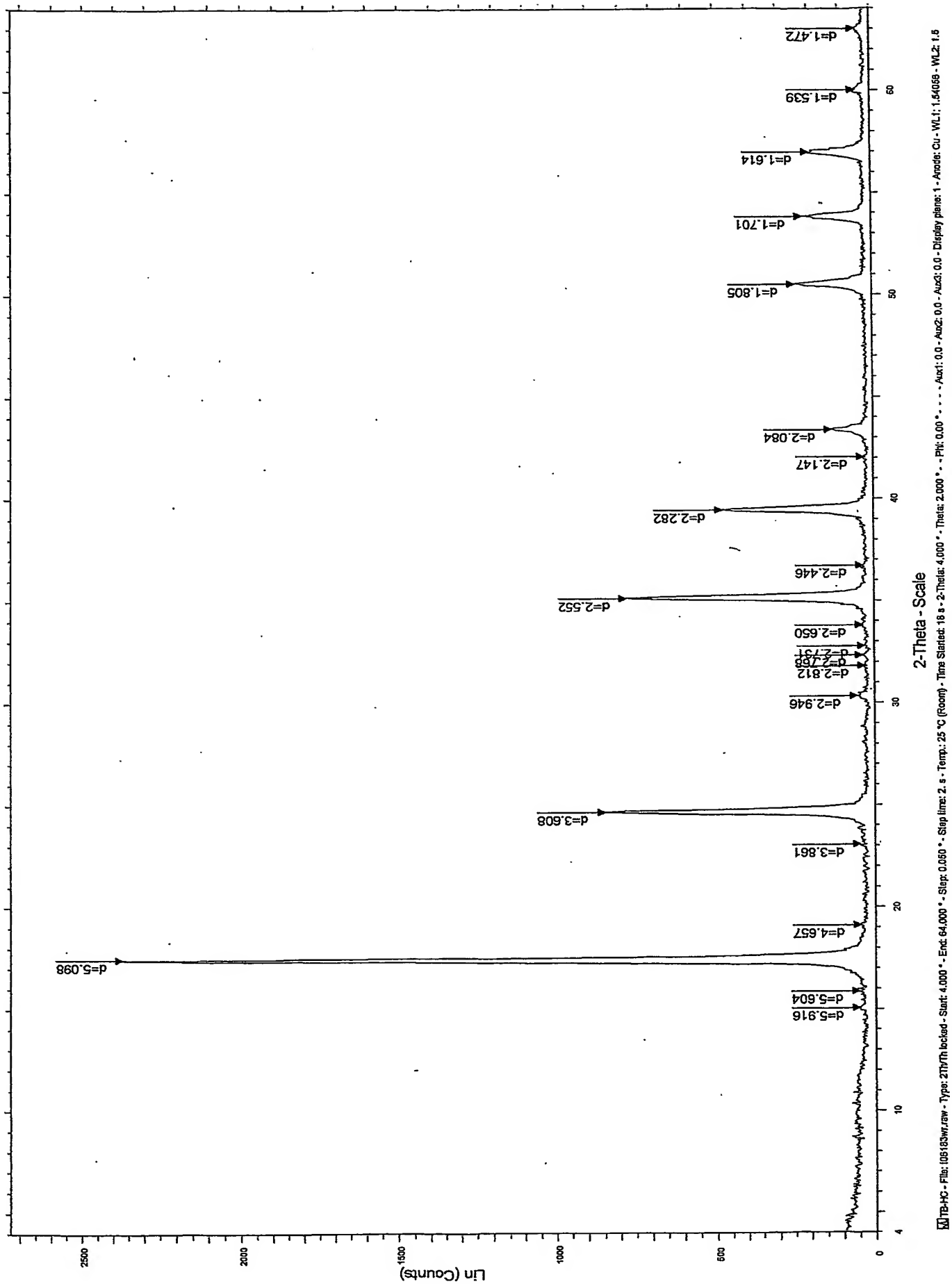
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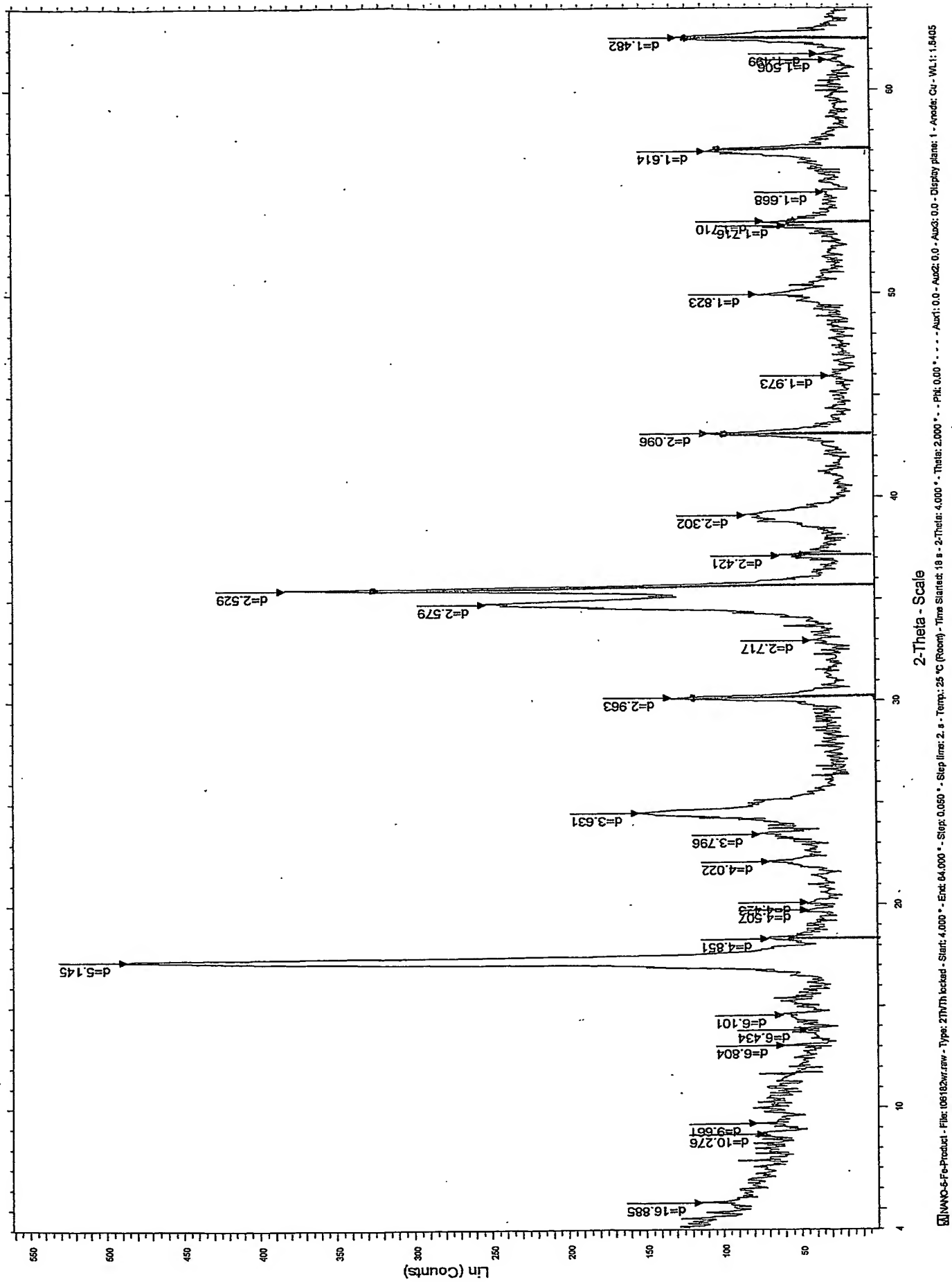
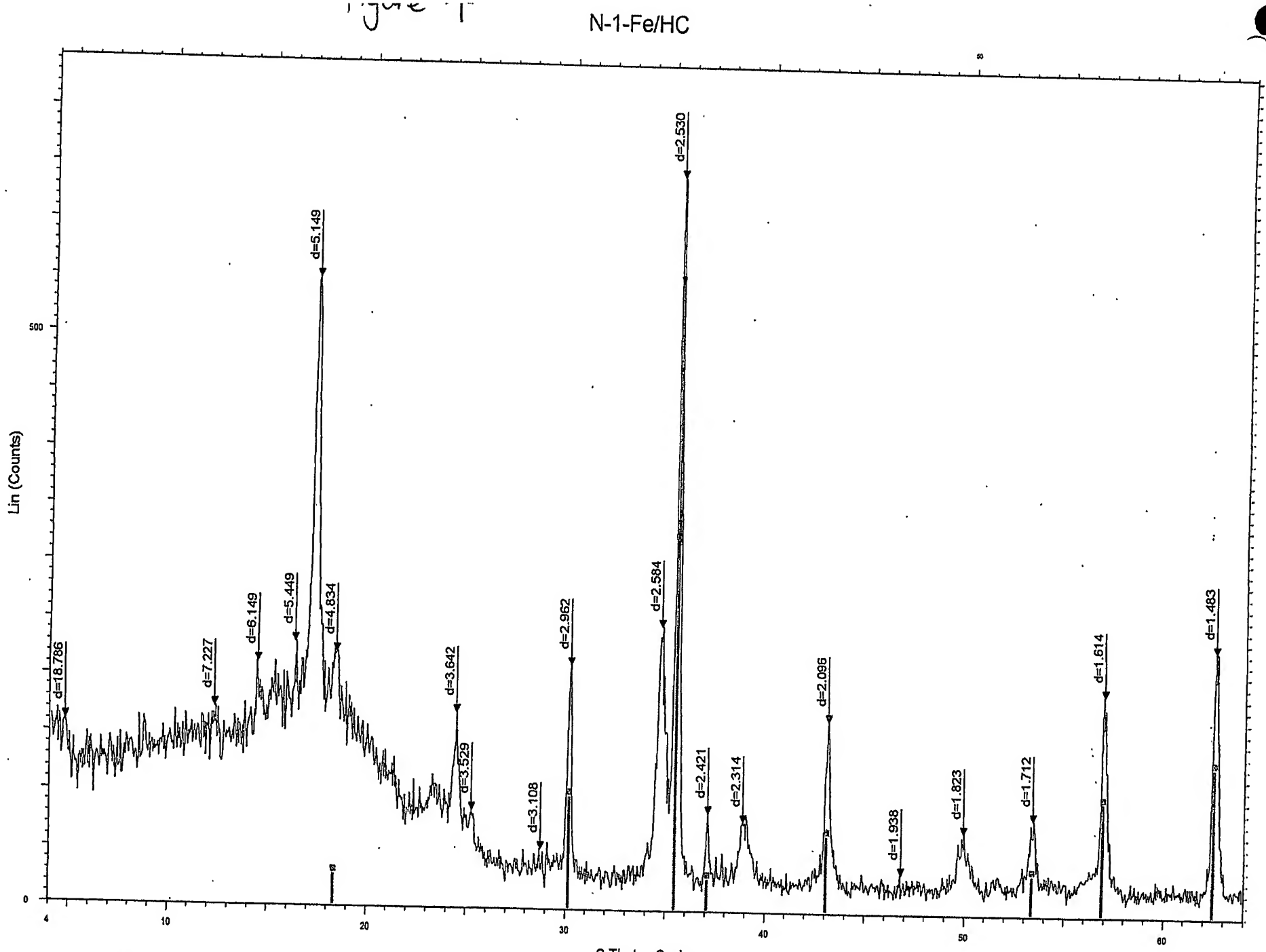
Figure 5

NANO-5-Fe-Product



under N_2 atmosphere, / O_2 in air

Figure 1



under AIR atmosphere / Fe only

4/10

Figure 5

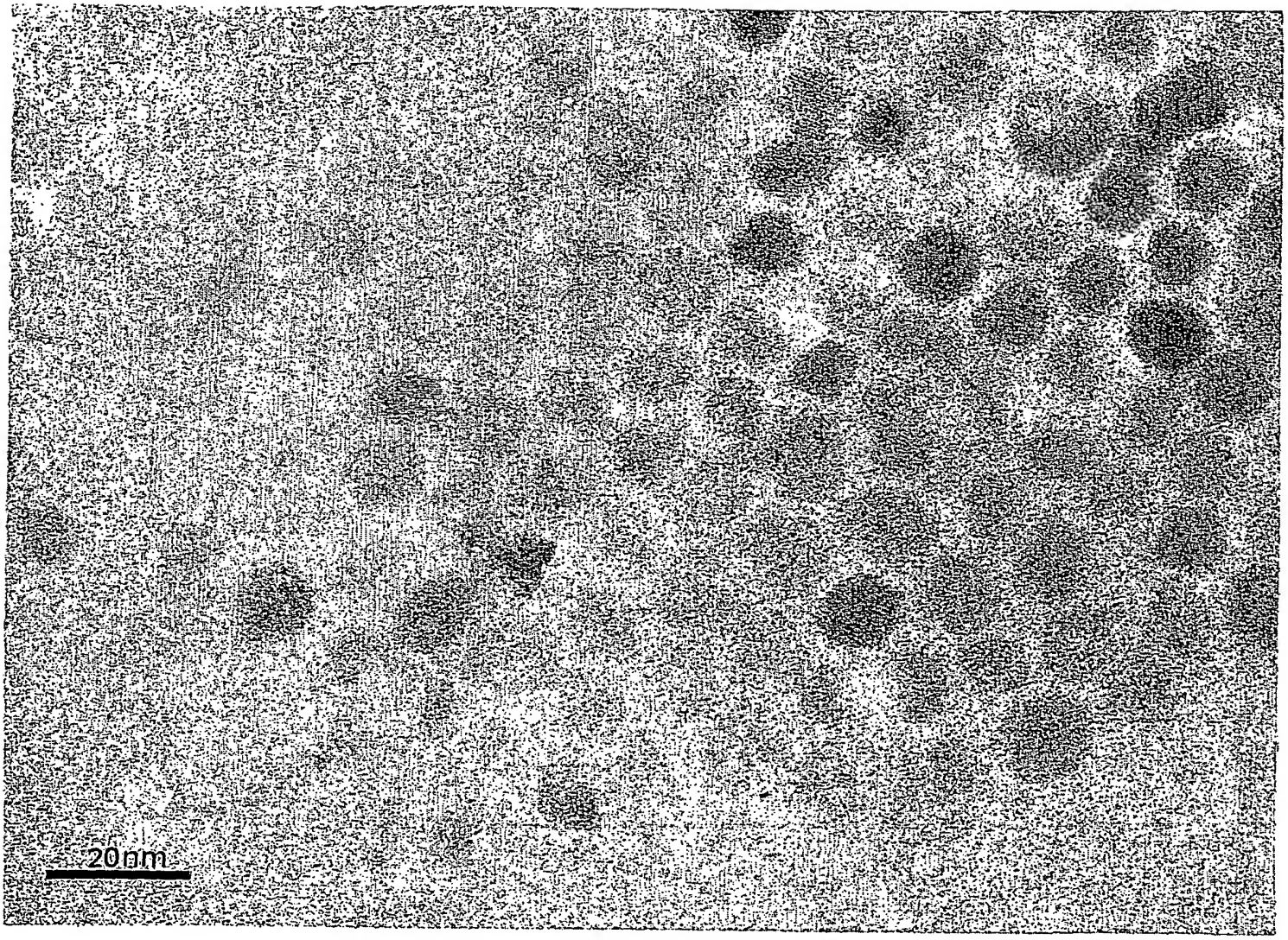


Fig 6

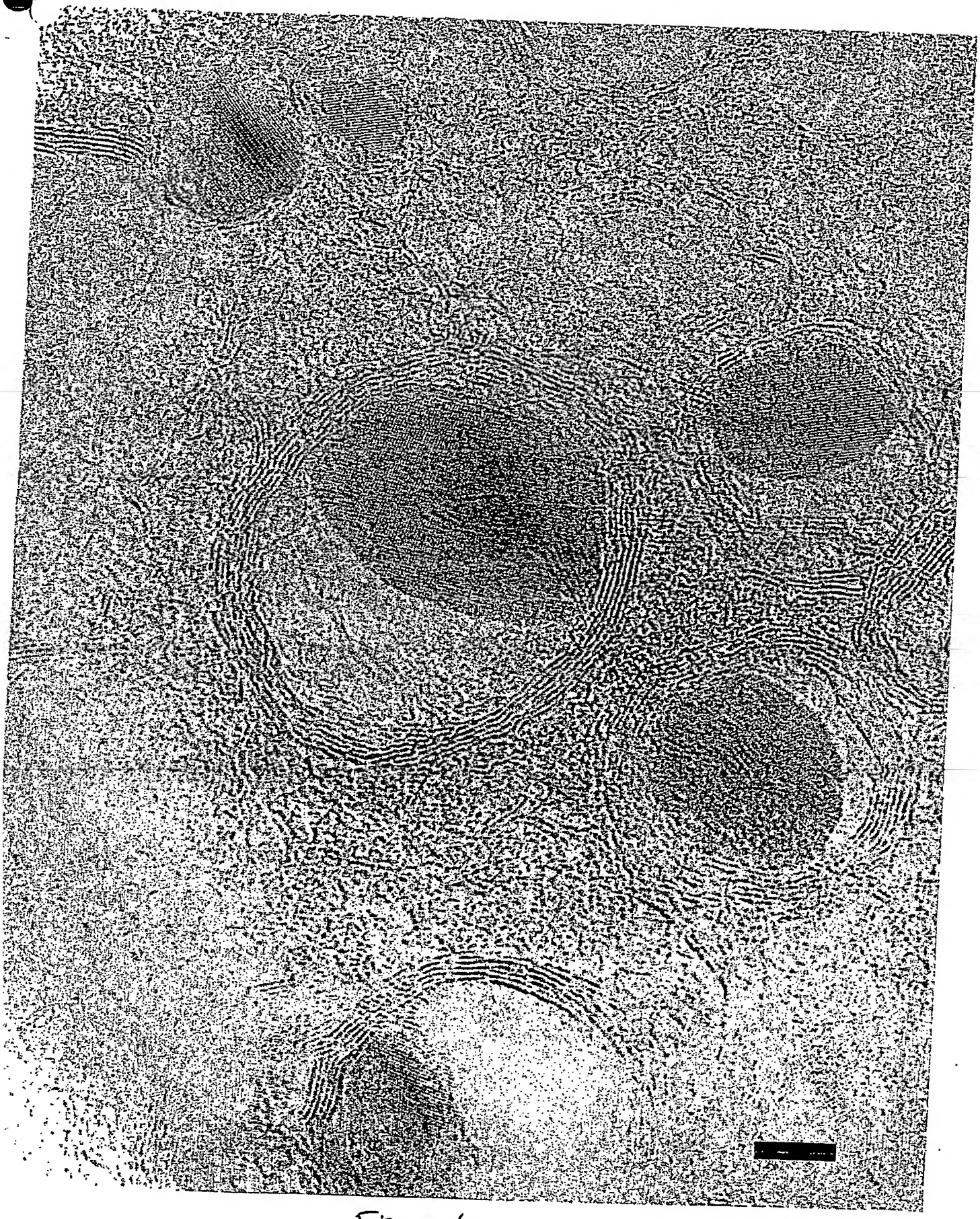
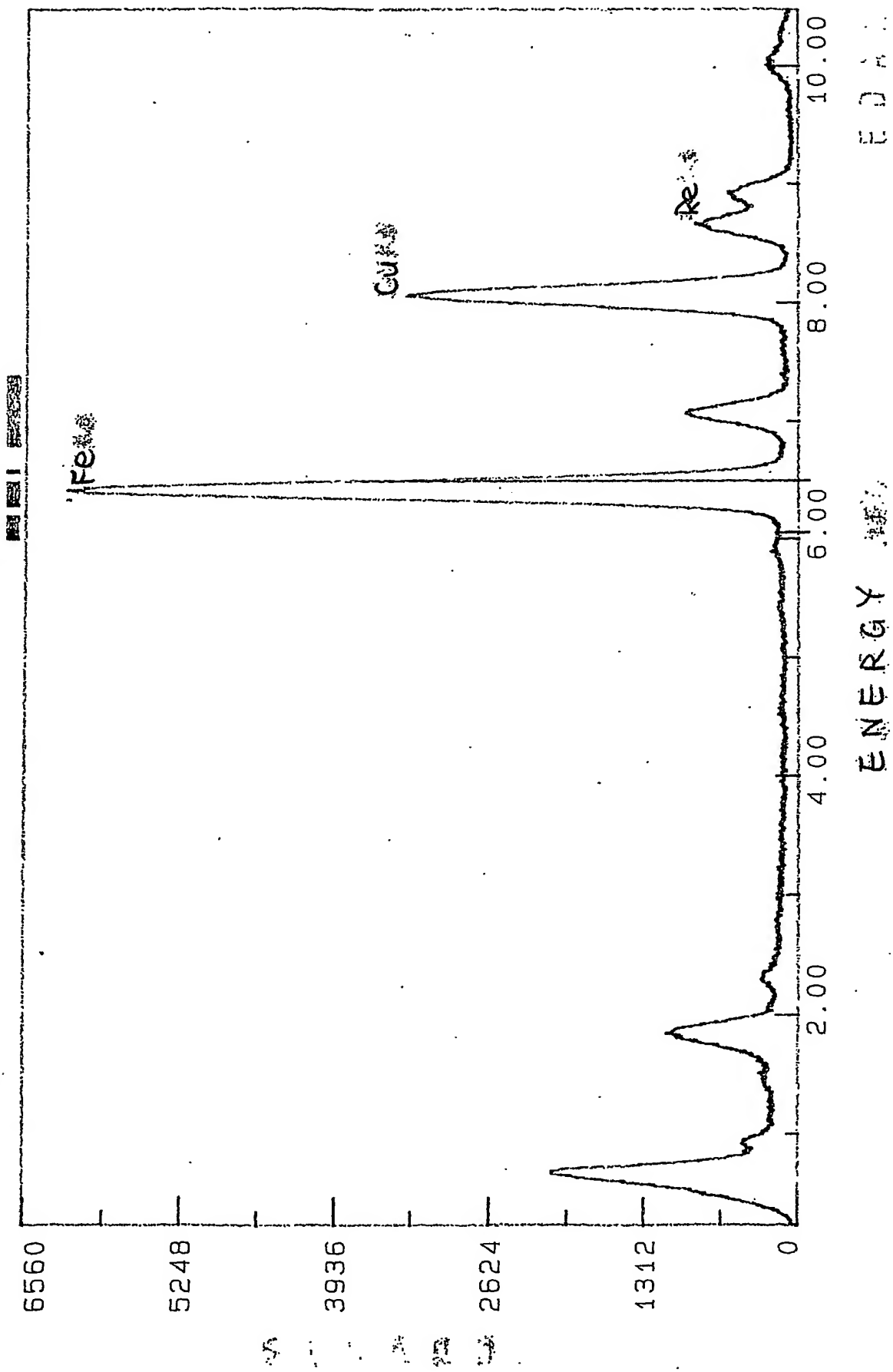


Figure 6

Figure 7



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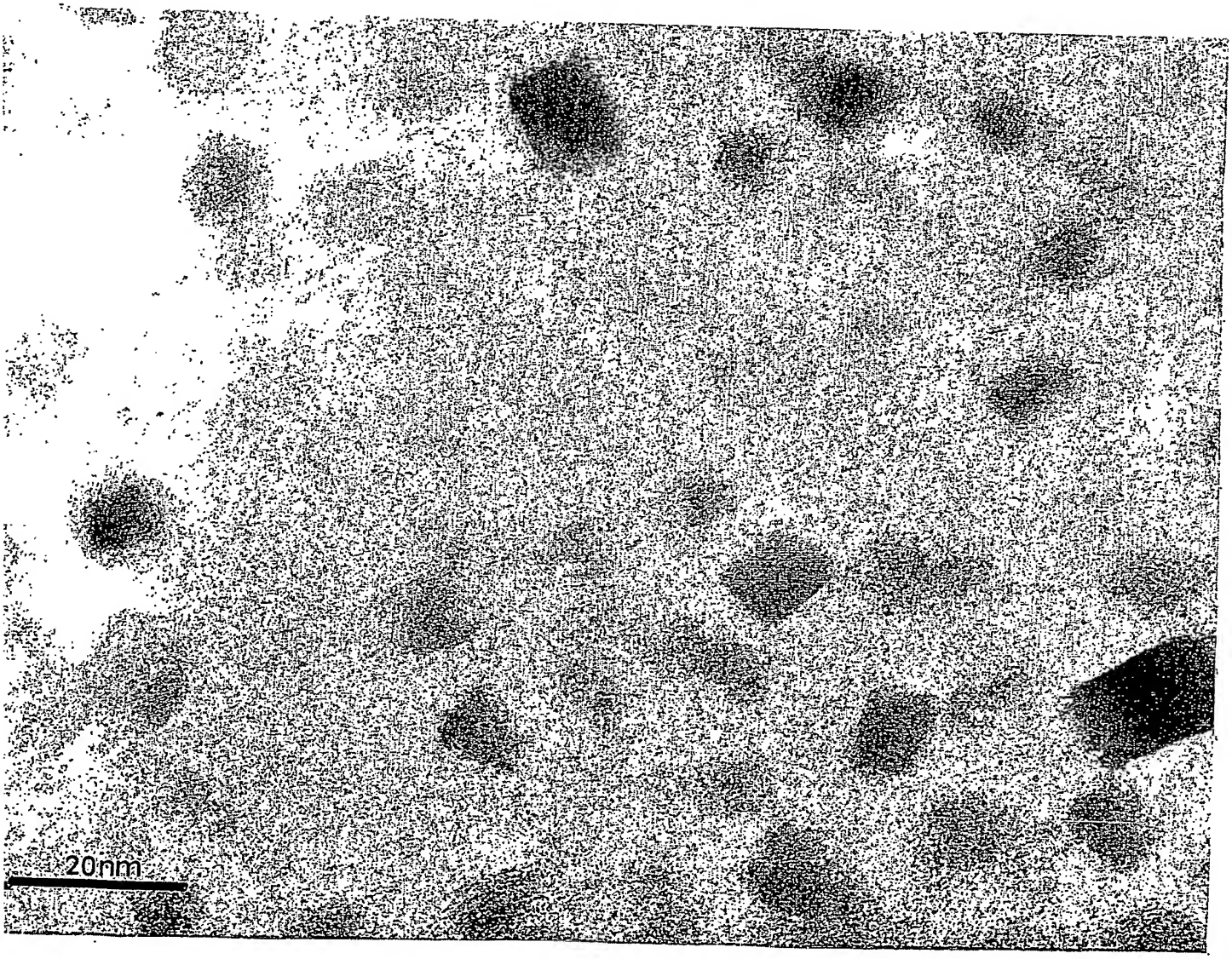

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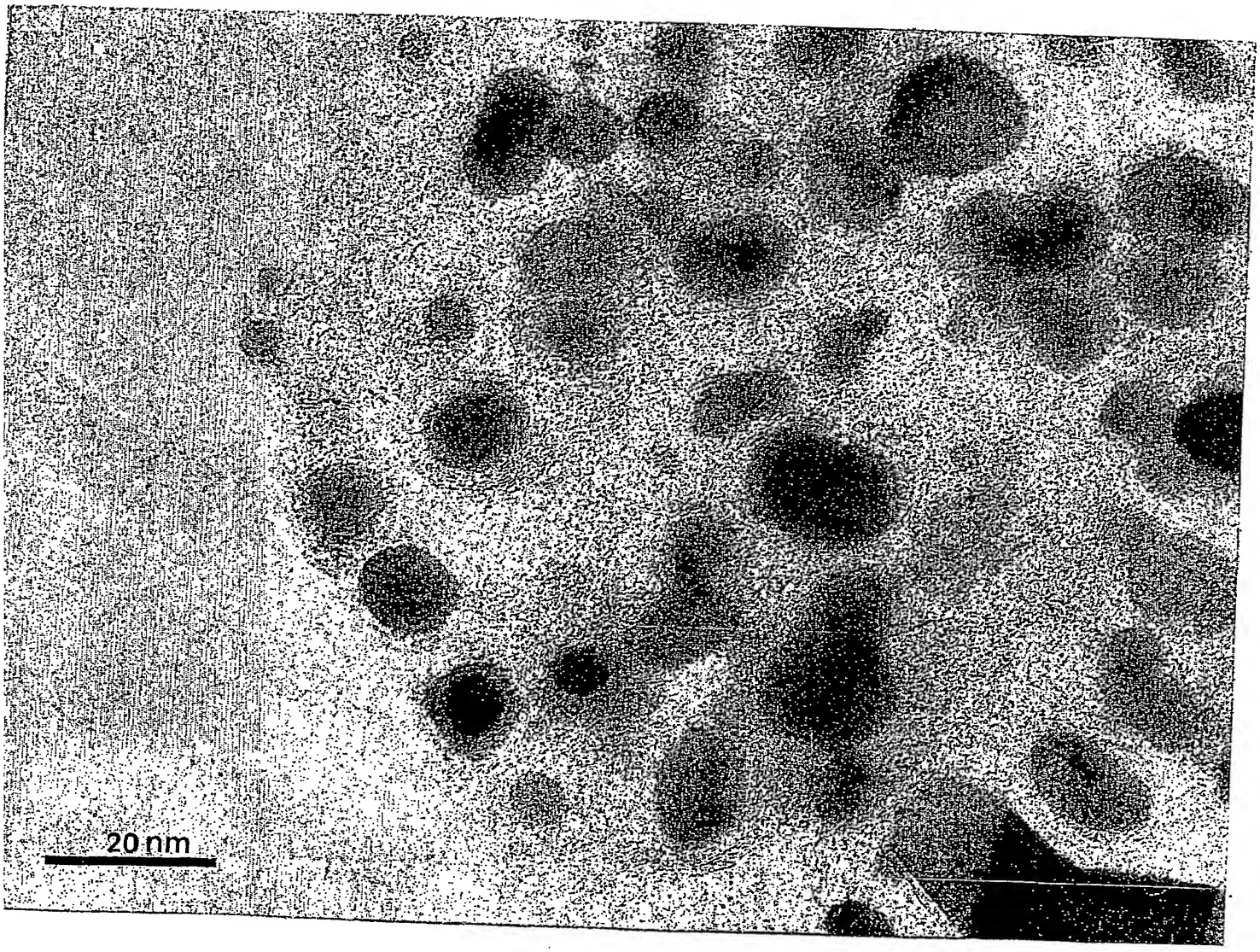

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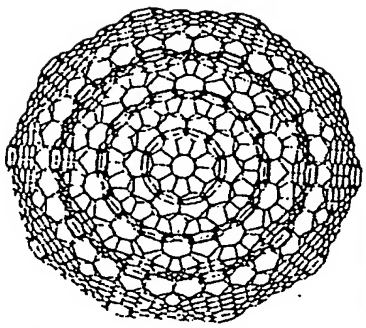
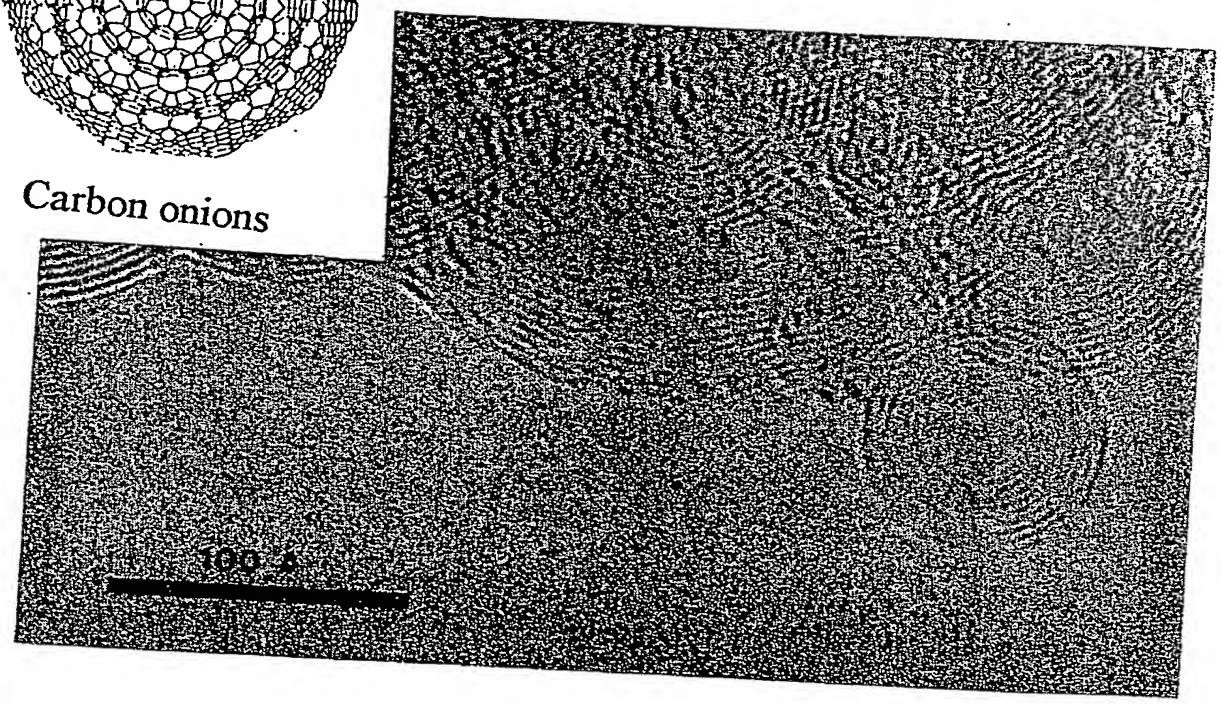


Carbon onions



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